

Remarks

Claims 1-19 are pending in the subject application. Submitted herewith is a Request for Continued Examination (RCE) under 37 CFR §1.114 for the subject application. By this Amendment, new claim 20 has been added. Support for the new claim can be found throughout the subject specification, including for example, at page 2, lines 18-21. Entry and consideration of the new claim presented herein is respectfully requested. Accordingly, claims 1-20 are currently before the Examiner for consideration. Favorable consideration of the pending claims is respectfully requested.

Claims 1-6 and 8-19 remain rejected under 35 USC §103(a) as obvious over Richardson *et al.* (WO 01/06004) in view of Gu *et al.* (U.S. Published Application No. 2003/0180737). In addition, claim 7 remains rejected under 35 USC §103(a) as obvious over Richardson *et al.* (WO 01/06004) in view of Gu *et al.* (U.S. Patent Application No. 2003/0180737) and further in view of Fend *et al.* (1999). The Examiner asserts that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to carry out first and second strand cDNA synthesis using the “single-pot” method of the Gu *et al.* publication when practicing the method of the Richardson *et al.* publication. Applicants respectfully traverse these grounds of rejection.

Applicants respectfully assert that the cited references, whether taken alone or in combination, do not teach or suggest the claimed invention. The Examiner asserts that it would have been obvious to adapt the method of the Richardson *et al.* publication so that the reverse transcription and amplification are carried out using the “single-pot” method of Gu *et al.* In order to establish a *prima facie* case of obviousness, it is necessary for the Patent Office to show that the ordinarily skilled artisan would have had some suggestion or motivation to combine the cited references. *In re Geiger*, 2 USPQ2d 1276 (Fed. Cir. 1987). The Examiner cites the *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727 (2007), as foreclosing the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. Applicants respectfully disagree and assert that the *KSR* decision did not preclude the requirement of a suggestion or motivation to combine or modify the teachings of art references in order to establish a *prima facie* case of obviousness. The *KSR* decision is limited to simple mechanical inventions

wherein a combination of elements that were well known in the art could easily be envisioned working together in a simple device. In that case, under those particular circumstances, then a teaching, suggestion, or motivation may not be required (although if the combination of well known elements would not necessarily yield a predictable outcome, then even for simple mechanical inventions a teaching, suggestion or motivation would be required). However, in all other cases, and particularly in complex and unpredictable arts such as chemistry and biotechnology, as in the instant application, then a teaching, suggestion, or motivation is still required and has not been obviated by the *KSR* decision.

Applicants respectfully maintain that the Examiner has not established that the cited references provide the requisite motivation to combine the teachings of the Richardson *et al.* and Gu *et al.* publications. The Examiner asserts that combining two steps from the teachings in the art into a single step would have been obvious and that a suggestion that the ordinarily skilled artisan would not have recognized the advantage of doing so assumes that the artisan would have “lacked common sense.” Applicants respectfully assert that the ordinarily skilled artisan would not have been able to predict the outcome of combining multiple chemical reaction steps into a single step. Absent such predictability, there must be a suggestion or motivation to combine the steps. The ordinarily skilled artisan would not have looked to combine the teachings of the Richardson *et al.* and Gu *et al.* publications as there was no teaching or suggestion in the art that such a combination would yield desirable results, or that it would even work at all. It is only the subject application that teaches the desirability and operability of the claimed method. Applicants again note that hindsight reconstruction of the prior art to arrive at Applicant’s invention is not permissible. *In re Sponnoble*, 160 USPQ 237, 243 (CCPA 1969).

Moreover, neither the cited references nor the Examiner provide any evidence that the results obtained with Applicants’ claimed invention were predictable from the cited publications or from the general knowledge of a person of ordinary skill in the art. The U.S. Supreme Court has indicated that a combination of elements is unlikely to be deemed obvious when the combined elements yield unpredictable or unexpected results. *KSR International Co. v. Teleflex Inc.*, *supra*. Applicants respectfully maintain that there are unexpected advantages and unpredictable results associated with Applicants’ claimed invention that are not suggested in, or that could not have been predicted from,

the cited publications or the general knowledge of the ordinary artisan. Applicants' claimed invention is simpler and more efficient, and requires fewer amplification cycles, than methods known in the art at the time of Applicants' invention. The advantages and unpredictable results associated with Applicants' claimed invention are clear to a person of ordinary skill in the art upon reading the subject application. There is nothing in the art that would lead an ordinarily skilled artisan to predict that Applicants' claimed invention would be more efficient or require fewer amplification cycles.

An invention that provides the discovery and solution to a problem that is not appreciated in the art is further evidence against a *prima facie* case of obviousness. *Eibel Process Co. v. Minnesota and Ontario Paper Company*, 261 US 45 (1923). As noted previously, Applicants' claimed invention solves problems that are not even addressed or recognized in the cited publications. For example, by comparison with the procedure in the Richardson *et al.* publication, the present invention avoids the need for rare restriction sites, and it allows for the inclusion of specific restriction sites for lambda cloning. Another advantage is that the production of complex products is minimized, due in part to the use of unique sequences in the heeled 5'-amplification and the heeled 3'-amplification primers which are absent from the genome being investigated. Moreover, while the procedure described in the Richardson *et al.* publication uses a single primer to amplify the products after reverse transcriptase and second strand synthesis, the present invention provides the significant advantage that two separate primers of unique sequence are used. In addition, Applicants' claimed invention not only provides greater amplification but also greater flexibility in use. For example, it readily allows the inclusion of specific restriction sites, for manufacturing subtracted normalized and enriched cDNA libraries, for fragmentation, and for use as probes on the microarrays and filters. It also allows the inclusion of specific restriction sites for lambda cloning, for the manufacture of single cell libraries. Thus, Applicants maintain that their claimed invention is not obvious over the cited publications. Accordingly, reconsideration and withdrawal of the rejections under 35 USC §103 is respectfully requested.

In view of the foregoing remarks, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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Attachment: Request for Continued Examination